longation of AV and VA conduction time were determined. The 1:1 AV and VA conduction cycle lengths before injection of adenosine were 340 ± 50 and 326 ± 75 msec, respectively. Adenosine induced dose-dependent prolongation of AV nodal conduction time and caused typical Wenckebach AV block in all 16 patients with EC_{50} and E_{max} values of 1.4 ± 0.8 mg and 54 ± 2%, respectively. Adenosine also induced dose-dependent prolongation of VA conduction time and VA block, however, with significantly ($P < 0.05$) higher EC_{50} and shorter E_{max}, i.e., 6.1 ± 1 mg and 20 ± 2%, respectively. The mean dose of adenosine to induce AV block is significantly lower than that to induce VA block (3.3 ± 1.6 vs. 7.7 ± 3.3 mg, $P < 0.05$). Notably, adenosine induced Wenckebach VA block in 10 of 16 patients and Mobitz type II block in 6 of 16 patients. In conclusion, adenosine is more potent in slowing AV than VA conduction, suggesting that the electrical wavefront entering the N zone of AV node is less affected by adenosine during VA than during AV conduction. In addition, retrograde fast pathway may at least in part involve conduction through the N zone of AV node.

2:30

798-3 A Comparison of Amiodarone versus Flecainide Using a Quinidine Standard in the Treatment of Resistant Chronic Atrial Fibrillation

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Chronic atrial fibrillation (AF) is a ommon arrhythmia with significant morbidity and mortality. The antiarrhythmic effects of amiodarone (AM) and flecainide (FLEC) in patients with resistant chronic AF have been studied separately in several small clinical trials. This study compared AM to FLEC in maintaining normal sinus rhythm (NSR) in patients (pts) with resistant chronic AF. To facilitate the comparison, quinidine (QUIN) was used as the reference standard.

Studies using AM or FLEC in the treatment of chronic AF refractory to either Class I AF drugs or sotalol were identified. The results of 6 trials of AM (200–400 mg/day; 315 pts) and 2 trials of FLEC (200–300 mg/day; 163 pts) were aggregated using meta-analysis in NSR at 3 and 12 mos for AM and FLEC were compared relative to corresponding results for QUIN, which were acquired from a meta-analysis of QUIN used as first-line therapy for AF.

Duration of chronic AF ranged from 2 wks to 25 yrs. After 3 and 12 mos of treatment with AM, 217 of 299 (72.6%) and 64 of 107 (59.8%) pts, respectively, remained in NSR. These percentages were significantly greater ($p < 0.0001$) when compared to QUIN at these time points (70% and 50%, respectively). After 3 and 12 mos of treatment with FLEC, the percentage of pts remaining in NSR were significantly lower ($p < 0.0001$) than QUIN: 79 of 163 (48.5%) and 56 of 163 (34%) pts, respectively. The aggregated percentages of pts requiring withdrawal of AM and FLEC were 9.5% and 8.6%, respectively. Mortality and proarrhythmia could not be assessed.

Conclusion: This analysis suggests that low-dose AM is more efficacious and equally well-tolerated when compared to FLEC in the management of chronic, drug-resistant AF.

2:45

798-4 Predictors of the Efficacy of Sotalol, a Class III Antiarrhythmic Agent, in the Treatment of Atrial Arrhythmias

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Sotalol, a class III antiarrhythmic drug (AAD) approved for use in ventricular arrhythmias, is being used with increasing frequency for supraventricular arrhythmias (SVA). To determine the efficacy of sotalol in the treatment of SVA and the predictors of sotalol failure or intolerance, 114 pts in whom sotalol was begun for SVA were reviewed. All pts had atrial fibrillation (109) and/or atrial flutter (32) (AF: paroxysmal in 76, chronic in 35), except for 3 who had SVT. Mean duration after diagnosis of SVA was 5.2 ± 8.2 yrs. The mean number of prior failed AADs was 1.96 ± 1.27 (range 0–6). Electrical cardioversion was achieved in 38/41 pts; 18 pts pharmacologically converted. Sotalol was stopped prior to discharge in 16 pts (inefficacy in 8, side effects in 4, prolonged QT in 2, and no longer indicated in 2). Prior to discharge, proarrhythmia occurred in 1 pt and bradycardia in 15 pts. 26 pts had prior pacemakers, and 11 pts required pacemakers for sotalol. Mean discharge dose was 229 ± 78 mg/day and mean discharge QTc was 462 ± 59 ms. Predictors for discontinuation of sotalol prior to discharge included degree of left atrial enlargement (LAE, $p = 0.03$) and QTc on sotalol ($p = 0.063$). Of 88 pts discharged on sotalol in sinus rhythm, 52 developed recurrent SVA (mean f/u 7.8 mos). After dose changes, 3 more pts became recurrence free. Of 36 recurrence-free pts, 12 had sotalol discontinued (side effects in 7, no longer indicated in 5). 2 pts discharged on sotalol developed proarrhythmia, and 2 pts died (1 noncardiac and 1 CVA). Overall, 27/114 pts (23.6%) begun on sotalol remained recurrence free and on the drug. Of 10 pts who began sotalol as first line antiarrhythmic therapy, 2 stopped sotalol in the hospital, 2 after hospital discharge, and 2 recurred after discharge (overall 40% recurrence free on sotalol). Univariate predictors of recurrent SVA on sotalol for pts discharged in NSR included younger age (60 ± 13 vs 68 ± 9 yrs, $p = 0.001$), longer duration since diagnosis of SVA (7.7 ± 11 vs 2.8 ± 4.0 yrs, $p = 0.009$), prior CABG ($p = 0.01$), number of failed AADs (2.4 ± 1.3 vs 1.4 ± 1.1, $p = 0.0003$), and shorter baseline QTc (441 ± 46 vs 465 ± 59 ms, $p = 0.049$) and discharge QRS (109 ± 32 vs 128 ± 41 ms, $p = 0.025$). Changes in HR or QTc were not significant predictors of sotalol success. Significant multivariate predictors of SVA recurrence adjusted for the follow-up period included number of failed AADs ($p = 0.0024$), discharge QRS ($p = 0.0038$) and age ($p = 0.03$). In summary, sotalol showed moderate (24%) efficacy in pts previously refractory to AADs and comparable efficacy as a first-line agent to that reported with other AADs. Changes in QT interval or HR could not be used to predict long term efficacy.

3:00

798-5 Risk of Initiating Antiarrhythmic Drug Therapy for Atrial Fibrillation

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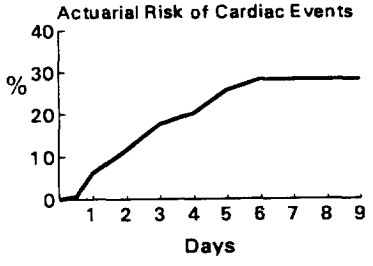
The side effects of antiarrhythmic drugs for atrial fibrillation (AF) are well recognized, but the incidence and time course of early events that justify observation in-hospital, are not well defined. Adverse cardiac events requiring intervention were determined for 169 consecutive hospitalized patients undergoing 253 trials of Class I or III antiarrhythmic drugs for AF. Patient characteristics were: age 64 (25–86) yrs, male 60%, structural heart disease 89% and prior myocardial infarction 18%. Adverse cardiac events occurred in 37 (15%) drug trials in 33 patients an average of 2.6 ± 1.1 days after initiation of therapy. The majority (65%) occurred within 3 days. The actuarial risk of cardiac events is shown in the Figure below. Of the 37 events, there were 26 (70%) bradyarrhythmias and 2 (5%) ventricular arrhythmias. Age, gender, and absence of structural heart disease were similar between patients with or without events. A previous history of myocardial infarction was associated with an increased risk of cardiac event (RR 2.1, $p = 0.06$). *Conclusion.* Bradyarrhythmias are the most common adverse cardiac event during initiation of drug therapy for AF. A strategy of hospitalization for electrocardiographic monitoring for 24–48 hours-after initiation of antiarrhythmic therapy is likely to miss some adverse cardiac events.



3:15

798-6 Acute Effects of Zatebradine on Cardiac Conduction and Repolarization in Anesthetized Dogs

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Zatebradine, a potent bradycardic agent, is believed to act selectively at the sinoatrial node. However, the selectivity of such an action relative to various electrophysiologic classes of action is not well defined. To characterize tie electrophysiologic properties of zatebradine, the corrected sinus node recovery time (SNRT/sinus cycle length), sinoatrial conduction time (SACT), conduction intervals, effective refractory period in atrium (AERP) and monophasic action potential duration (APD_{90}) in ventricle were measured before (Ctrl) and after administration of incremental doses of zatebradine (Zat, 0.1–1.5 mg/kg) in 15 anesthetized dogs. The effects of zatebradine on various electrophysiologic parameters could be observed immediately after a single i.v. bolus and reached steady-state at 15 min.

Results (Mean ± S.D.):